

WE CLAIM:

1. A method for acoustically depositing a fluid on a surface of a cell sample, comprising:
 - (a) providing a reservoir containing a fluid;
 - (b) positioning the cell sample surface in droplet-receiving relationship to the reservoir; and
 - (c) applying focused acoustic energy in a manner effective to eject a droplet of the fluid from the reservoir such that the droplet is deposited on the sample surface at a designated site.
2. The method of claim 1, wherein the cellular sample comprises cells from a cellular culture.
3. The method of claim 1, wherein the cellular sample is a tissue.
4. The method of claim 3, wherein the tissue is an animal tissue.
5. The method of claim 4, wherein the animal tissue is mammalian tissue.
6. The method of claim 1, wherein surface of the cellular sample is compositionally nonuniform.
7. The method of claim 1, wherein the fluid is an analysis-enhancing fluid.
8. The method of claim 1, wherein the analysis-enhancing fluid comprises a detectable label moiety.
9. The method of claim 8, wherein the label moiety is a fluorescent moiety.

-33-

10. The method of claim 8, wherein the label moiety is a magnetic moiety.
11. The method of claim 8, wherein the label moiety is a radioactive moiety.
- 5 12. The method of claim 1, wherein the fluid contains a biomolecule.
13. The method of claim 12, wherein the biomolecule is peptidic.
14. The method of claim 12, wherein the biomolecule is nucleotidic.
- 10 15. The method of claim 12, wherein the biomolecule is enzymatic.
16. The method of claim 1, wherein the fluid contains cellular matter.
- 15 17. The method of claim 16, wherein the cellular matter comprises at least one whole cell.
18. The method of claim 16, wherein the cellular matter comprises at least one cell extract.
- 20 19. The method of claim 6, wherein the fluid is selected to preferentially interact with selected moieties on the compositionally nonuniform sample surface.
- 25 20. The method of claim 7, further comprising, after step (c), (d) subjecting the sample to conditions effective to allow the analysis-enhancing fluid to interact with the sample surface so as to render the sample surface suitable for analysis.
21. The method of claim 20, wherein the analysis-enhancing fluid comprises an analysis-enhancing moiety and a carrier fluid.

30

-34-

22. The method of claim 21, wherein the carrier fluid is evaporated from the sample surface in step (d).

5 23. The method of claim 20, wherein the analysis-enhancing fluid is solidified on the sample surface in step (d).

24. The method of claim 23, wherein the analysis-enhancing fluid comprises a mass-spectrometry matrix material.

10 25. The method of claim 24, wherein the mass-spectrometry matrix material is a photoabsorbing matrix material.

26. The method of claim 20, further comprising, after step (d), (e) analyzing the sample at the designated site.

15 27. The method of claim 26, further comprising, after step (d) and before step (e), (d') applying effective energy to the designated site to release sample molecules from the sample surface for analysis.

20 28. The method of claim 27, wherein the energy applied in step (d') is effective to ionize the sample molecules released from the sample surface.

29. The method of claim 28 wherein step (d') comprises bombarding the designated site with photons.

25 30. The method of claim 29, wherein photonic bombardment is carried out using a laser.

30 31. The method of claim 26, wherein step (e) comprises determining the molecular weight of the sample molecules.

32. The method of claim 26, wherein step (e) comprises determining the extent of any interaction between the analysis-enhancing fluid and the sample surface.

5 33. The method of claim 1, wherein step (c) is repeated to deposit a plurality of droplets on the sample surface.

34. The method of claim 33, wherein the droplets are deposited on the sample surface at a single designated site.

10 35. The method of claim 33, wherein the droplets are deposited on the sample surface at different designated sites.

15 36. The method of claim 35, wherein the different designated sites form an array.

37. The method of claim 36, further comprising, after step (c), (d) subjecting the sample to conditions effective to allow the fluid to interact with the sample surface at the different designated sites so as to render the sample surface suitable for analysis.

20 38. The method of claim 37, further comprising, after step (d), (e) analyzing the composition of the sample at each designated site.

25 39. The method of claim 38, further comprising, during or after step (e), (f) preparing a compositional map of the cellular sample surface using the analysis of step (e).

40. The method of claim 1, wherein step (a) comprises providing a plurality of reservoirs, each containing a different analysis-enhancing fluid; and step (c) comprises applying focused acoustic energy in a manner effective to eject a droplet of fluid from

each reservoir such that the droplets from the reservoirs are deposited on at least one designated site on the sample surface.

41. The method of claim 40, wherein droplets of different analysis-enhancing
5 fluids are deposited on the sample surface at a single designated site.

42. The method of claim 41, wherein the droplets are deposited on the sample surface at different designated sites.

10 43. The method of claim 42, further comprising, after step (c), (d) subjecting the sample to conditions effective to allow the fluid to interact with the sample surface at the different designated sites so as to render the sample surface suitable for analysis.

44. The method of claim 43, further comprising, after step (d), (e) analyzing the
sample at each designated site.

45. The method of claim 44, wherein the different designated sites form an array.

20 46. The method of claim 45, further comprising, during or after step (e), (f)
preparing a compositional map of the cellular sample surface using the analysis of step
(e).

47. A system for acoustically depositing a fluid on a surface of a cellular sample, comprising:

25 a reservoir containing a fluid;

an acoustic ejector comprising an acoustic radiation generator for generating acoustic radiation and a focusing means for focusing the acoustic radiation generated;

an acoustic ejector positioning means for positioning the acoustic ejector in acoustic coupling relationship to the reservoir;

30 a cellular sample having a surface; and

-37-

a sample positioning means for positioning the cellular sample surface such that at least one designated site thereon is in droplet-receiving relationship to the reservoir.

48. The system of claim 47, wherein the fluid is an analysis-enhancing fluid.

5

49. The system of claim 48, wherein the analysis-enhancing fluid comprises a mass-spectrometry matrix material.

10 50. The system of claim 49, wherein the mass-spectrometry matrix material is a photoabsorbing matrix material.

51. The system of claim 48, wherein the analysis-enhancing fluid is selected to interact preferentially with selected moieties on the sample surface.

15 52. The system of claim 48, wherein the analysis-enhancing fluid comprises a detectable label moiety.

53. The system of claim 47, further comprising an analyzing means for analyzing the composition of the sample at a designated site.

20

54. The system of claim 53, wherein the analyzing means comprises a mass spectrometer.

25 55. The system of claim 53, wherein the analyzing means comprises a detector selected from the group consisting of optical detectors, radiation detectors, and magnetic detectors.

30 56. The system of claim 53, further comprising an energy applying means for applying energy to the at least one designated site to effect release and ionization of sample molecules from the sample surface for analysis.

57. The system of claim 56, wherein the energy applying means comprises a photon bombarding means for bombarding the at least one designated site with photons.

5 58. The system of claim 57, wherein the photon bombarding means comprises a
laser.

59. The system of claim 47, wherein the sample positioning means is adapted to controllably position the sample such that a plurality of designated sites on the cellular sample surface are successively placed in droplet receiving relationship to the reservoir.

60. The system of claim 59, wherein the designated sites form an array.

61. The system of claim 47, wherein the cellular sample surface is substantially planar.

62. The system of claim 47, further comprising at least one additional reservoir, wherein each reservoir contains a different fluid.

20 63. The system of claim 62, comprising a single ejector, wherein the acoustic
ejector positioning means is adapted to position the acoustic ejector in acoustic coupling
relationship to each of the reservoirs.

64. A method for analyzing a surface of a cellular sample, comprising:

25 (a) providing a reservoir containing an analysis-enhancing fluid;
(b) positioning the cellular sample surface such that a designated site on the cellular sample surface is in droplet-receiving relationship to the fluid containing reservoir, wherein the designated site is one of a plurality of designated sites within an array of such sites;

-39-

(c) applying focused acoustic energy in a manner effective to eject a droplet of the fluid from the reservoir such that the droplet is deposited on the sample surface at the designated site;

5 (d) repeating steps (b) and (c) with each different designated site so that at least one droplet is deposited at each designated site;

(e) applying energy to each of the designated sites to effect release of sample molecules therefrom; and

(f) analyzing the released sample molecules.

10 65. The method of claim 64, wherein step (f) comprises performing mass spectrometric analysis on the sample molecules.

15 66. The method of claim 65, further comprising during or after step (f), producing a compositional map of the cellular sample surface from the results of the mass spectrometric analysis.

67. A system for acoustically depositing a fluid on a surface of a cellular sample, comprising:

20 a reservoir containing an analyte-enhancing fluid;
an acoustic ejector comprising an acoustic radiation generator for generating acoustic radiation and a focusing means for focusing the acoustic radiation generated;

an acoustic ejector positioning means for positioning the acoustic ejector in acoustic coupling relationship to the reservoir;

25 a cellular sample having a surface;
a sample positioning means for positioning a cellular sample surface such that a plurality of different designated sites within an array of such sites on the cellular sample surface are successively placed in droplet-receiving relationship to the reservoir;

an energy applying means for applying energy to the designated sites to effect release and ionization of sample molecules therefrom; and

30 an analyzing means for analyzing the sample molecules from the designated sites

Atty Dkt 7610-0042.21
PATENT

-40-

68. The system of claim 67, wherein the energy applying means comprises a photon bombarding means for bombarding the designated site with photons.

5 69. The system of claim 68, wherein the photon bombarding means comprises a laser.

70. The system of claim 69, wherein the analyzing means comprises a mass spectrometer.

10